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09/401,636	09/22/1999	LARS T. HELLMAN	10223/006001	4922

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MARK S ELLINGER
FISH & RICHARDSON
60 SOUTH SIXTH STREET
SUITE 3300
MINNEAPOLIS, MN 55402

EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	25

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/401,636	Applicant(s) HELLMAN, LARS T.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- Th MAILING DATE of this communication appears on th cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The request filed on 4/15/02 for continued examination under 37 C.F.R. § 1.17 (e) is acknowledged.

2. Claims 25-54 are pending and being acted upon in this Office Action.

3. In view of the amendment filed 4/15/02, the following objection and rejections remain.

4. The disclosure is objected to because of the following informalities: (1) SEQ ID NO is required under 37 CFR.1.821(d) in the Description of the Drawings for Fig 1, and Fig 2A-B, (2) the Description of Drawing for Fig 2A-B does not correspond to the Figure itself, in which Figures labeled as Fig 2a, Fig 2a1 Fig 2a2, Fig 2b, Fig 2b1 and Fig 2b2, and (3) Fig 3A, filed 4/19/02, is missing. It is suggested that Applicant amend the Description of the Drawings to correspond to the Figures mentioned above. Appropriate action is required.

5. Claims 53 and 54 are objected to because they depend on non-existing claim 58.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 25-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for immunogenic polypeptides such as the ones shown in Fig 2 consisting of a self IgE CH3 domain from rat, human, mouse, dog or pig and one or more non-self IgE domains such as IgE CH2 domain from opossum, or platypus and IgE CH4 domain from opossum or wombat for induce anti-self IgE response in a mammal for treating atopic allergies, **does not** reasonably provide enablement for (1) *any* immunogenic polypeptide, comprising a self IgE CH3 domain and one or more non-self IgE domains, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein at least one of said non-self IgE domains "**comprises**" an IgE sequence present in *any* "**non-placental mammal**" such as koala, kangaroo,

and wallaby, and (2) *any* immunogenic polypeptide comprising a self IgE domain and one or more non-self IgE domains wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal and wherein said at least non-self IgE domains "**comprises**" an IgE sequence present in *any* "non-placental mammal" such as koala, kangaroo, and wallaby for treating *any* disease such as infections. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only immunogenic polypeptides such as the ones shown in Fig 2 comprising a self IgE CH3 domain from rat, human, mouse, dog or pig and one or more non-self IgE domains such as IgE CH2 domain from opossum, or platypus and IgE CH4 domain from opossum or wombat for induce anti-self IgE response in a mammal.

The specification does not teach how to make and use *any* immunogenic polypeptides mentioned above wherein at least one of said non-self IgE domains "comprises" an IgE sequence present in *any* "non-placental mammal" for treating *any* infectious diseases. The term "comprises" is open-ended. It expands the non-self domains to include additional amino acid at either or both ends, in addition to the amino acids which already in the non-self IgE CH2 and CH4 domains. There is no guidance in the specification as to what type and number of amino acids can be added and whether after addition of amino acids that the immunogenic polypeptide would retain both structure and function such as stabilizes the functional conformation of the self-IgE CH3 domain since the CH3 domain is critical for IgE binding to the high affinity FcεRI. Further, the specification discloses non-self IgE CH2 and IgE CH4 domains from only three non-placental mammals such as opossum, platypus and wombat. There is no disclosure as to the structure of *any* IgE CH2, and IgE CH4 domains from *any* other non-placental mammals such as koala, kangaroo, and wallaby.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Given the indefinite number of undisclosed immunogenic polypeptide, comprising a self IgE CH3 domain and *any* one or more non-self IgE domains, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* undisclosed "non-placental mammal" such as koala, kangaroo, and wallaby, it is unpredictable which undisclosed immunogenic polypeptide would be useful for inducing even anti-self IgE response in a mammal, let alone treating *any* infection.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

8. Claims 25-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* immunogenic polypeptide, comprising a self IgE CH3 domain and one or more non-self IgE domains, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein at least one of said non-self IgE domains "**comprises**" an IgE sequence present in *any* "**non-placental mammal**" such as koala, kangaroo, and wallaby, and (2) *any* immunogenic polypeptide comprising a self IgE domain and one or more non-self IgE domains wherein said

immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal and wherein said at least non-self IgE domains "**comprises**" an IgE sequence present in *any* "non-placental mammal" such as koala, kangaroo, and wallaby for treating *any* disease such as infections.

The specification discloses only immunogenic polypeptides such as the ones shown in Fig 2 comprising a self IgE CH3 domain from rat, human, mouse, dog or pig and one or more non-self IgE domains such as IgE CH2 domain from opossum, or platypus and IgE CH4 domain from opossum or wombat for induce anti-self IgE response in a mammal.

With the exception of the specific immunogenic polypeptides such as the ones shown in Fig 2, there is insufficient written description about the structure associated with function of *any* immunogenic polypeptide, comprising a self IgE CH3 domain and *any* one or more non-self IgE domains "**comprises**" an IgE sequence present in *any* "non-placental mammal" such as koala, kangaroo, and wallaby for treating infection. The term "comprises" is open-ended. It expands the domain to include additional amino acids at either or both ends, in addition to the amino acids already in the non-self domain. Further, the specification discloses non-self IgE domains from only three species of non-placental mammal such opossum, platypus and wombat, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 48-49 and 52-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Nissim *et al* (EMBO J 10(1): 101-107, 1991; PTO 892).

Nissim *et al* teach a polypeptide such as CHM3 mutant comprising a self mouse IgE CH3 domain and one or more non-self IgE domain such as human IgE CH1, CH2 and CH4 domains

wherein the reference polypeptide lacks light chain Ig sequence (See page 102, chimeric human-mouse IgE, Fig 1, page 103, column 1, first full paragraph, in particular). The reference polypeptide inherently induces an anti-self response in a mammal. The term "comprising" is open-ended. It expands the claimed polypeptide to include additional amino acids at either or both ends to read on the reference polypeptide. The reference polypeptide wherein one of the non-self IgE domains is an IgE CH2 and IgE CH4 domain and wherein the self IgE domain is located between the reference IgE CH2 and CH4 domains (See Fig 1, CHM3, in particular). Claim 53 is included in this rejection because one of the reference non-self IgE domains is an IgE CH2 domain. Claim 54 is included in this rejection because one of the reference non-self IgE domains is an IgE CH4 domain. Thus, the reference teachings anticipate the claimed invention.

11. Claims 25-26, 29, 31, 48-49 and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by US Pat No 5,653,980 (Aug 1997; PTO 892).

The '980 patent teaches a polypeptide comprising the amino acid sequence (the entire sequence or part thereof) of the constant CH2-CH3 domains of IgE that lacks the CH1 domain from mammalian species such as human and rat wherein the reference IgE domains are mutated by exchange (self versus non-self) fused to glutathione-S-transferase (Sj26) from *S japonicum* (See column 4, lines 21-26, column 9, lines 22-26, in particular). The reference polypeptide lacks light chain Ig sequences and the reference polypeptide is effective to induce anti-self IgE response in a mammal such as rat (See column 10, example 2, in particular). The term "comprising" is open-ended. It expands the claimed polypeptide to include additional amino acids at either or both ends to read on the reference polypeptide. Claim 29 is included in this rejection because it is an inherent properties that the reference immunogenic polypeptide capable of dimerizing since it contains a cysteine residue at 328 in the Fc region, which is responsible for interchain disulfide bond. Claim 49 is included in this rejection because the reference polypeptide is for immunizing human, which used in a vaccine to induce an anti-self IgE response in human. Claims 31 and 53 is included in this rejection because one of the reference non-self IgE domains is an IgE CH2 domain. Claim 53 depends on claim 58 is an error, the examiner has considered claim 53 depends on base claim 48. Thus, the reference teachings anticipate the claimed invention.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 33-34 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 5,653,980 (Aug 1997; PTO 892).

The teachings of the '980 patent have been discussed supra.

The claimed invention as recited in claim 33 differs from the reference only by the recitation that the immunogenic polypeptide comprising one or more non-self IgE domains and an N-terminal half of a self IgE CH3 domain, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal.

The '980 patent teaches there is a risk that antibodies directed against the N-terminal part of the CH2 domain or the C-terminal part of CH3 domain may give rise to an anaphylactic shock in the mammals in which the antibodies are formed (See column 6, lines 36-39, in particular).

From the teachings as discussed supra, it would have been obvious to one of ordinary skill in the art at the time the invention was made to exclude the C-terminal part of CH3 domain as taught by the '980 patent for an immunogenic polypeptide comprising one or more non-self IgE domains and an N-terminal half (excluding the C-terminal half) of the self IgE CH3 domain, for immunogenic polypeptide that is effective to induce an anti-self IgE response in a mammal.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because the '980 patent teaches antibodies directed against the C-terminal part of CH3 domain may give rise to an anaphylactic shock in the mammals minimize the risk of generating anaphylactic response (See column 6, lines 36-39, in particular) to minimize the risk of generating anaphylactic response.

14. Claims 27-28, 35-36, 41, 43 and 50-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nissim *et al* (EMBO J 10(1): 101-107, 1991; PTO 892) or US Pat No 5,653,980 (Aug 1997; PTO 892).

The teachings of Nissim *et al* and the '980 patent have been discussed supra.

The claimed invention as recited in claims 27, 35, 41 and 50 differs from the reference only by the recitation that at least one of said non-self IgE domains comprises and IgE sequence present in a non-placental mammal.

The claimed invention as recited in claims 28, 36, 43 and 51 differs from the reference only by the recitation that non-placental mammal is selected from the group consisting of opossum platypus, and wombat

However, non-placental mammals such as opossum, platypus, and wombat are the most evolutionary distantly related mammals to placental mammals such as humans and would be the most obvious choice as a source of distantly related non-self IgE.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the non-self IgE domains from placental mammals as taught by Nissim *et al* or the '980 patent for the IgE domains from the most evolutionary distantly related non-placental mammals such as opossum, platypus, and wombat for an immunogenic polypeptide comprising at least one of said non-self IgE domains comprises and IgE sequence present in a non-placental mammal such as opossum, platypus, and wombat.

One of ordinary skill in the art at the time the invention was made would have been motivated to use non-self IgE because nonplacental mammals are the most distantly related mammals to placental mammals and would be the most obvious choice as a source of distantly related non-self IgE.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
July 1, 2002

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600